Uncovering addiction

By Michael Parrish

Without a doubt, addiction and substance abuse represent a devastating, pervasive problem for both individuals and society as a whole. According to the National Institute on Drug Abuse, substance abuse costs the country more than 600 billion dollars annually.[1] While this statistic is astounding, it does not adequately convey the emotional effects of drug abuse and its effects on public safety.

Fortunately, investigators from a broad range of disciplines, including neuroscience and psychology, are working to design and test treatment plans that will help mitigate the effects of drug abuse. One such research group is the Cognition and Addiction Biopsychology lab (CABlab) of UNC-Chapel Hill led by Dr. Charlotte Boettiger, professor of psychology and principal investigator of the CABlab. Dr. Boettiger's researchers use cognitive neuroscience tools, such as neuroimaging and genetic analysis, to explore the neurobiology of addiction. As stated by Dr. Boettiger, translational science labs such as the CABlab "lay the groundwork for testing substance abuse therapies."[2] The CABlab is helping uncover specific behaviors and cognitive phenotypes associated with addiction. One of the lab's most significant contributions to the field is discovering "factors that can interact with acute pharmacological agents."[1] By analyzing different genotypes and cognitive phenomena correlated with addiction, pharmaceutical companies and therapy designers will better understand which neural systems to target.Understanding how the brain interfaces with drugs is key to effectively implementing addiction research. The human brain has complex networks of neurons designed to reinforce naturally beneficial behaviors such as eating and drinking. However, drugs can take advantage of these life-sustaining motivational circuits by altering synaptic activity and global brain function. Simply put, synapses are the functional units for communication in the nervous system. To maintain healthy, adaptive behavior in humans, neurons and their synapses must perform controlled regulation of the chemical events during neurotransmission.

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Dr. Charlotte Boettiger

Christopher Smith

If any of the steps in neurotransmission are altered, behavioral and psychological consequences will emerge. Many prescription and recreational drugs function by exploiting a certain step in neurotransmission; for example, cocaine and several other drugs affect synaptic transmission by blocking reuptake of the neurotransmitter dopamine. Understanding exactly how synapses are modulated by drug use and what specific regions of the reward circuitry are affected is the subject of intense research in neuroscience. Most relevant to the CABlab's research is the goal of correlating this neurobiological activity with specific addictive or impulsive behaviors.

Cognitive traits and behaviors are formed by a complex interaction of conditions and factors such as age, sex, and genetics. Isolating certain factors that may cause particular individuals to be prone to addictive behaviors and impulsive decision making is a research goal of CABlab graduate student Christopher Smith. Smith was inspired to pursue a career in addiction research after experiencing the effects alcohol had on a family member.[3] He specifically investigates the neurobiology associated with now-versus-later decision making. This "delay-discounting" behavior relates to choosing between immediate and delayed rewards. The discounting task used in the CABlab's experiments focuses on subjects choosing between hypothetical monetary amounts with time delays. An example is deciding between five dollars today or ten dollars in six months. Moreover, the process of delaying reward receipt can be conceptualized as being disrupted in addiction. For instance, a substance abuser may favor immediate positive effects of administering a drug now over the delayed reward of not being hungover as a result of drug use the following morning. As such, persons with previous diagnosis of an alcohol abuse disorder are more likely to value "now" over "later" in this discounting task.

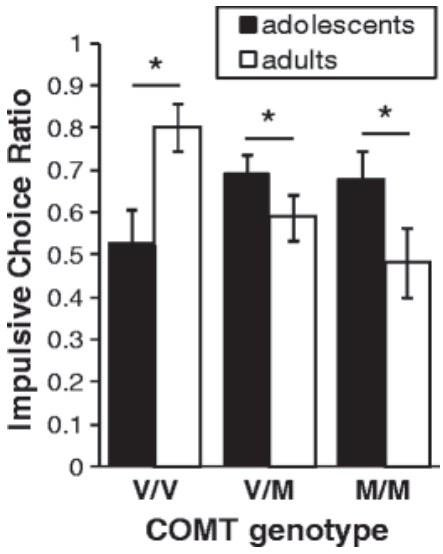

Figure 1. *This bar graph shows how the interaction between age and COMT genotype influences impulsive decision-making. The x-axis is labeled with the three genotypes associated with the COMT Val158Met polymorphism. The y-axis represents the ratio of impulsive choices to total task choices. Image courtesy of Christopher Smith.*

Calculating Cost

Estimated annual costs in the US, in billions[1]

Alcohol abuse: $235
Tobacco abuse: $193
Illicit drug abuse: $193
TOTAL: more than $600

Recently, Smith's work led to an advance in the understanding of how age interacts with the COMT Val158Met genotype. His findings, published in the journal Psychopharmacology earlier this year, show that frontal dopamine signaling and delay discounting are modulated by both the COMT genotype and developmental changes from adolescence to young adulthood (Figure 1).[4] The function of COMT under normal conditions is to degrade catecholamines, such as dopamine, in the prefrontal neural synapses. According to Smith's article, the specific COMT genetic polymorphism studied in the CABlab "results in a fourfold reduction of COMT enzymatic activity." Looking ahead, Smith says that he hopes to start using "the tools of magnetic resonance imaging (MRI) and ultimately positron emission tomography (PET) to better understand the neurobiology of now-versus-later decision making and the role of dopamine in this behavior."[3]

Chris Smith and Dr. Boettiger's research is just one example of the many attempts being made to better understand the neurobiology of abnormal behaviors caused by addiction. As a result of this type of scientific investigation, treatment plans will be optimized to account for differences in genotype and age so that more individuals around the globe can lead successful, fulfilling lives.

References

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3. Interview with Christopher T. Smith, 9/20/12.
4. Smith, C.T.; Boettiger, C.A. *Psychopharmacology* 2012, 222, 609-617.